May 8, 2003

Prakash Surana, Ph.D.
Product Stewardship Coordinator
Celanese Ltd.
1201 Anise Court
Freeburg, IL 62243

Dear Dr. Surana:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 1,3-Butanediol posted on the ChemRTK HPV Challenge Program Web site on January 15, 2003. I commend Celanese Ltd. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Celanese Ltd. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-*S*-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
1,3-Butanediol

SUMMARY OF EPA COMMENTS

The sponsor, Celanese Ltd., submitted a test plan and robust summaries to EPA for 1,3-butanediol dated December 17, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 15, 2003. Analog data were also included for ecological and human health effects.

EPA has reviewed this submission and has reached the following conclusions:

1. Analog Justification. Although analog data are presented for ecological and human health endpoints, no justification is given in either case. The submitter needs to provide this justification before the chemicals can be considered as appropriate analogs for 1,3-butanediol.

2. Physicochemical Properties and Environmental Fate. Adequate data are available for these endpoints. However, the submitter needs to provide a robust summary for the ready biodegradation study described in the test plan.

3. Health Effects. Adequate data were provided for the acute, repeated-dose, and developmental toxicity endpoints for the purposes of the HPV Challenge Program. However, EPA reserves judgement on the genetic toxicity endpoint, pending receipt of an adequate justification for the use of 1,4-butanediol as an analog. Also, the submitter needs to revise the robust summary for the 'five-generation' reproductive toxicity study before the adequacy of the data can be determined.

4. Ecological Effects. The toxicity endpoint for algae has been adequately addressed for the purposes of the HPV Challenge program. However, the fish and daphnia endpoints are inadequately addressed because the submission lacks justification for the use of analog data and lacks key robust summary information.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE 1,3-BUTANEDIOL CHALLENGE SUBMISSION

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Vapor Pressure. This endpoint has been adequately addressed. However, the test plan reports 0.027 hPa @ 20°C while the summary reports .027 hPa @ 25°C. The submitter needs to correct the discrepancy.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Adequate data are available for all endpoints.

Photodegradation. This endpoint has been adequately addressed for indirect photolysis. However, the submitter should provide information as to whether these compounds are expected to absorb sunlight at > 290 nm.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data were provided for the acute, repeated-dose, and developmental toxicity endpoints for the purposes of the HPV Challenge Program. However, EPA reserves judgement on the genetic toxicity endpoint, pending receipt of an adequate justification for the use of 1,4-butanediol as an analog. The submitter needs to address this and other deficiencies in the robust summaries and significantly revise the robust summary for the 'five-generation' reproductive toxicity study.

Genetic Toxicity. Although the 1,4-butanediol studies submitted for gene mutations and chromosomal aberrations appear to be well-conducted, the submitter's justification for using analog data for bacterial mutagenicity stated only that 'simple glycols as a class are not known to be genotoxic.' No studies were cited to show that various types of glycols (e.g., 1,2; 1,3; 1,4) are negative in the Ames test. Additional acceptable justification for the use of 1,4-butanediol data might include comparative metabolism information or comparison of general toxicities.

Reproductive Toxicity. EPA reserves judgment on the 'five-generation' reproductive toxicity study in dietarily-exposed rats pending the submission of additional information in the robust summary. (This study is considered to be the key study because it included multiple dose levels.) The summary omitted the compound purity, methods for evaluating toxicity in parents (e.g., it is not clear whether the epididymides were analyzed), the specific reproduction and lactation parameters that were measured (e.g., were the number of implantation sites recorded?), and statistical methods. In addition, the summary defined the study type as a 5-generation study, although the summary appears to describe a 3-generation study (5 litters/generation). The similarity of the study to OECD Guideline 416 could not be determined from the information provided.

Ecological Effects (fish, invertebrates, and algae)

The endpoint for algae has been adequately addressed for the purposes of the HPV Challenge Program. However, the justification for using analog data for the fish and invertebrate endpoints has not been clearly stated. In addition, the submitter needs to provide robust summaries for the key fish and invertebrate analog studies before EPA can determine whether these data are adequate.

Fish. The submitter needs to address several discrepancies between the values reported in the test plan and robust summary for the predicted acute fish toxicity of 1,3-butanediol. In the test plan (p. 10) the submitter reported a 96-hour LC_{50} of 8984 mg/L, but reported a 96-hour LC_{50} of 9484 mg/L in the robust summary (p. 8). Additionally, these values differed from the predicted value (9494 mg/L) that is provided by ECOSAR (v0.99) when the log K_{ow} for 1,3-butanediol (-0.29) is entered into the program, as was reportedly done by the submitter.

Invertebrates. The submitter reported a predicted 48-hour EC_{50} of 7344 mg/L in the test plan (p. 10), but 8684 mg/L in the robust summary (p. 8). The submitter explained the derivation of the robust summary value (*i.e.*, entry of the log K_{ow} for 1,3-butanediol into the ECOSAR program); however, it is not clear how the test plan value was derived.

Specific Comments on the Robust Summaries

Many robust summaries did not provide enough detail to evaluate the studies. The submitter should consult EPA guidance documents for the preparation of robust summaries (http://www.epa.gov/opptintr/chemrtk/guidocs.htm). In addition, each summary should clearly identify the test substance by the chemical name. Finally, the reference list should provide a complete citation for each article.

Environmental Fate

Biodegradation. The submitter needs to provide a robust summary of the ready biodegradation study described in the test plan (Reference # 11; Huntingdon Life Sciences Limited, 2000).

Health Effects

Genetic Toxicity. A robust summary for a negative cytogenetics/chromosomal aberrations assay in rats exposed in a multigenerational feeding bioassay omitted the name and purity of the test material. The submitter needs to indicate whether the animals were adults when the bone marrow was taken; also, the number of animals assessed in each generation is limited (2/sex/dose) compared with OECD Guideline 475, which specifies 5/sex/dose. Despite these deficiencies, the data are acceptable when considered in addition to the chromosomal aberrations study on 1,4-butanediol (if adequate justification is provided for the analog).

Developmental Toxicity. The developmental toxicity data are acceptable. However, the robust summary for a study in rats exposed by gavage omitted the gavage vehicle, maternal necropsy data (if performed), and mortality data.

Ecological Effects

Invertebrates. ECOSAR predicts a 48-hour LC_{50}, not a 48-hour EC_{50}, for this chemical class. Thus, the submitter needs to change "EC_{50}" to "LC_{50}" in the robust summary.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.